

**REMARKS**

Claims 32, 39, 42, and 49 have been amended for greater clarity. Support for the claim amendments can be found throughout the specification and original claims. Specifically, support for the recitation “dual cleavage restriction enzyme” is found, for example, on page 15, lines 13-19. Support for the recitation “excised from said vector” is found, for example, on page 15, lines 25-26. No new matter has been introduced.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Applicants note that the Examiner has withdrawn the rejections under 35 U.S.C. § 102(b) and § 103(a) in view of Applicants’ Response filed on October 5, 2005.

**Request for Withdrawal of Finality**

As a first point, Applicants note that the rejection under 35 U.S.C. § 102(a) is a new ground of rejection. Although the Office Action alleges that the new ground for rejection was necessitated by Applicants’ previous amendments, Applicants disagree with this assessment.

In Applicants’ previous response, Applicants amended claims 32, 37, and 42 solely to improve the clarity of the claims and to further satisfy the requirements of 35 U.S.C. § 112, second paragraph. Specifically, Applicants amended the claims to more particularly point out that the originally recited term “restriction site” refers to “recognition site.” Thus, the claim remained virtually unchanged with regard to the claimed recombinant vector. It was clear to one of skill in the art that the claims referred to “recognition site(s)” for a restriction enzyme. Accordingly, if the present rejection under 35 U.S.C. § 102(a) is relevant to the currently pending claims, it was relevant to the previously pending claims and could have been raised in the prior Office Action. In fact, the prior Office Action broadly construed the term “restriction site” and did not read any limitations from the specification into the claims. Given that the rejection was not necessitated by Applicants’ previous amendment and could have been raised in the prior Office Action, the present Office Action should not have been made final. MPEP 706.07(a).

In view of the above, reconsideration and withdrawal of the finality of the Office Action and entry of this amendment are respectfully requested.

Rejections of Claim 32-35, 37-46, and 48-51 under 35 U.S.C. § 112, First Paragraph

Claims 32-35, 37-46, and 48-51 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner asserts that “Applicants’ claims are directed to a broad genus recombinant vectors (*e.g.*, viral, plasmid, etc.) that can infect host cells of any type (*e.g.*, human, bacterial, yeast, etc.) via any mechanism (*e.g.*, replicate, integrate, etc.). In addition, although said vectors must contain one or more recognition sites for a restriction enzyme, no limitation is placed on the type of restriction enzyme that may be used (*e.g.*, class I, class II, class IIs, etc.). Applicants’ specification provides only one example of a pSP-luc+ plasmid [containing] U1 and BaeI “double cleavage” restriction site *i.e.*, BaeI/U1 construct.” See Office Action, page 3, lines 8-15.

Applicants respectfully traverse this rejection.

Applicants have amended independent claims 32 and 42 to more particularly point out certain embodiments of the invention. Applicants’ amendments are not made in acquiescence to the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

Applicants reiterate that where, as in this case, (1) the inventive portion of the subject matter is disclosed and (2) any additional variability within the genus arises due to additional elements that are not part of the inventor’s contribution, and when the level of knowledge and skill in the art would allow one skilled in the art to recognize that the applicant was in possession of the genus, the written description cannot be deemed defective. See Written Description Guidelines Training Materials available at, <http://www.uspto.gov/web/offices/pac/writtendesc.pdf> (released March 1, 2000, Example 8, page 35).

In this case, independent claim 32 as amended is directed to a recombinant vector comprising an isolated nucleotide sequence encoding an snRNA, wherein said nucleotide sequence has been modified to contain one or more recognition sites for a restriction enzyme,

such that digestion with a single restriction enzyme excises from said vector a restriction fragment which includes said recognition site and forms insertion sites in said vector, wherein the restriction enzyme is a dual cleavage restriction enzyme. Independent claim 42 as amended is directed to a recombinant vector comprising an isolated nucleotide sequence encoding an snRNA, wherein said nucleotide sequence comprises an insertion cassette between two insertion sites, wherein said two insertion sites are formed by digestion with a single restriction enzyme to excise from said vector a restriction fragment that contains a recognition site for said restriction enzyme, wherein the restriction enzyme is a dual cleavage restriction enzyme, and wherein said insertion cassette comprises a modification fragment comprising a nucleotide sequence complementary to a target.

One of skill in the art would know that the inventive portion of the claimed recombinant vector lies in the unique merging of technological features known in the art. For example, digestion with a single restriction enzyme excises from said vector a restriction fragment which includes said recognition site and forms insertion sites in said vector. As the specification sufficiently describes these characteristics of the genus of the claimed recombinant vectors of the invention (see, *e.g.*, page 15, lines 13-29; page 16, lines 1-26; Example on pages 21-23), a skilled artisan would recognize that Applicants were in possession of the claimed invention.

Applicants further point out that at the time this application was filed, snRNAs and vectors for encoding nucleotide sequences such as snRNAs were known and understood. In accordance with the written description guidelines and the MPEP, “[i]nformation which is well known in the art need not be described in detail in the specification.” Written Description Guidelines for the Examination of Patent Applications, section II, page 1105, column 3; MPEP 2163.

For the above reasons, Applicants maintain that all pending claims are supported by the specification with sufficient detail, and in light of the detailed description provided in the specification and the high level of skill in the art of molecular biology, that Applicants were in possession of the claimed invention at the time this application was filed. Accordingly, reconsideration and withdrawal of rejection are respectfully requested.

Objections to Claims 49 and 50

The Examiner points out that claim 49 depends from claim 47 which has been canceled. In response, Applicants have amended claim 49 to correct claim dependency, thereby obviating this objection.

Rejections of Claims 32-34 and 41 under 35 U.S.C. § 102(a)

Claims 32-34 and 41 are rejected under 35 U.S.C. § 102(a) over Vidaver *et al.* (Genetics, November 1999, 153, 1205-1218). Applicants respectfully traverse this rejection and contend that the rejection is moot in light of the amended claims.

Specifically, the Examiner asserts that Vidaver *et al.* disclose a PCR product which has been modified to contain a FokI recognition site “such that digestion with a single restriction enzyme (i.e., FokI) will excise a restriction fragment from the modified nucleotide sequence . . . which includes said recognition site and forms insertion sites in said nucleotide sequence.” See Office Action, page 11, lines 3-13.

The Examiner takes the position that a fragment that would be produced from the digestion of an “unincorporated” nucleotide sequence meets all of the currently claimed limitations because “the claimed ‘restriction fragment’ need not be ‘excised’ from ‘the vector’ (e.g., claim 32 doesn’t read ‘. . . such that digestion with a single restriction enzyme excises a restriction fragment which includes said recognition site and forms insertion sites in said vector’) . . .” See Office Action, page 12, lines 4-11.

As described above, Applicants have amended independent claim 32 to clarify that digestion with a single restriction enzyme excises from said vector a restriction fragment which includes said recognition site and forms insertion sites in said vector. Applicants submit that the pending claims as amended are not anticipated by Vidaver *et al.*

Vidaver *et al.* disclose a PCR product containing a FokI recognition site and digestion of the PCR product with the FokI restriction enzyme (see, e.g., page 50, lines 28-29). First, Applicants note that unlike the instantly recited nucleic acid sequence, Vidaver’s PCR product containing the FokI recognition site is not present on a vector. Further, as the FokI

restriction enzyme binds to a recognition site GGATG and cleavages 9 and 13 base-pairs away from the recognition site in a staggered fashion, digestion with the FokI restriction enzyme excises from the PCR product a restriction fragment which does not include the recognition site for FokI. Accordingly, Vidaver *et al.* fail to teach the invention as recited in claim 32.

For the above reasons, Applicants submit that independent claim 32 as well as claims dependent thereon are novel and not obvious in view of the teachings of Vidaver *et al.* because Vidaver *et al.* do not teach or suggest all the elements of the invention of claim 32. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejections of Claims 32-34, 41-42, 44-46, 48, and 51 under 35 U.S.C. § 103(a)

Claims 32-34, 41-42, 44-46, 48, and 51 are rejected under 35 U.S.C. § 103(a) over Noonberg *et al.* (WO 95/10607) in view of Cease *et al.* (Biotechniques 14(2): 250-5, 1993). Applicants respectfully traverse this rejection.

Applicants contend that the pending claims are not obvious over the cited references. Applicants note that the Examiner has withdrawn the novelty rejection and acknowledged that Noonberg *et al.* do not teach all the elements of the claimed invention. In particular, the Examiner admits that “[f]or claims 32 and 42, Noonberg *et al.* fail to disclose a modified nucleotide sequence that upon digestion with a single restriction enzyme would excise a restriction fragment that includes the recognition site. Noonberg *et al.* only disclose the use of SmaI, which would destroy the recognition site (i.e., cleavage is CCC↓GGG)” (see Office Action, page 15, lines 9-12). Applicants submit that Noonberg *et al.* fail to teach the unique class of restriction enzymes (*e.g.*, BaeI) and their corresponding recognition sites present on the claimed recombinant vector. As recited, the recited restriction enzymes are such that digestion with a single restriction enzyme excises from said vector a restriction fragment which includes said recognition site and forms insertion sites in said vector.

Cease *et al.* fail to bridge the gap between Noonberg *et al.* and the claimed invention as recited in amended claims 32 and 42. Cease *et al.* teach use of recognition sites of class II restriction enzymes FokI and BbsI in a vector for PCR cloning. However, as the FokI and

BbsI restriction enzymes cleave a few base-pairs away from their recognition sites in a staggered fashion, digestion with either FokI or BbsI restriction enzyme excises a restriction fragment which does not include the recognition site for FokI or BbsI (see Figure 2), contrary to the Examiner's assertion. Instead, the recognition site for FokI or BbsI is still present on the vector after digestion with FokI or BbsI restriction enzyme.

Therefore, Applicants submit that none of these cited references teach or suggest all the claim limitations. Even if combined, the proposed combination still does not teach all the elements of the invention of claim 32 or 42. Thus, at least one requirement for establishing a *prima facie* case of obviousness has not been satisfied.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 32-34, 41-42, 44-46, 48, and 51 under 35 U.S.C. 103(a).

Rejections of Claims 32-35, 41-46, 48, and 51 under 35 U.S.C. § 103(a)

Claims 32-35, 41-46, 48, and 51 are rejected under 35 U.S.C. § 103(a) over Noonberg *et al.* (WO 95/10607) and Cease *et al.* in view of the alleged admission of prior art in the specification, Cohen *et al.* (Proc. Natl. Acad. Sci. 91: 10470-10474, 1994), and Tuschl *et al.* (EMBO 17: 2637-2650, 1998). Applicants respectfully traverse this rejection.

Applicants note that although claims 32-35, 41-46, 48, and 51 are rejected based on this ground, the reasons provided by the Examiner are directed to dependent claims 35 and 43 only. Specifically, the Examiner asserts that the combined references of Noonberg *et al.* and Cease *et al.* teach all the limitation of claims 32-35, 41-46, 48, and 51. However, the Examiner acknowledges that the combined references of Noonberg *et al.* and Cease *et al.* do not teach the limitations of claims 35 or 43 (see Office Action, page 17, lines 11-20).

Applicants have explained above that the combined references of Noonberg *et al.* and Cease *et al.* do not teach all the elements of the claimed invention. Specifically, these two cited references, singly or in combination, fail to teach the unique class of restriction enzymes (*e.g.*, BaeI) and their corresponding recognition sites present on the claimed recombinant vector recited in independent claims 32 and 42. None of the other cited references (Cohen *et al.* and Tuschl *et al.*) bridge the gap between the combined references of Noonberg *et al.* and

Cease *et al.* and the claimed invention. Accordingly, all the cited references fail to teach or suggest all the elements of the claimed invention as recited in independent claims 32 and 42, as well as all claims depending from these claims.


Thus, at least one requirement for establishing a *prima facie* case of obviousness has not been satisfied. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a).

**CONCLUSION**

In view of the foregoing amendments and remarks, the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Please charge any deficiency or credit any overpayment in the fees that may be due in this matter to **Deposit Account No. 18-1945, under Order No. WIBL-P01-523.**

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Respectfully submitted,

By   
Lisa M. Treannie

Registration No.: 41,368  
ROPES & GRAY LLP  
One International Place  
Boston, Massachusetts 02110-2624

(617) 951-7000  
(617) 951-7050 (Fax)  
Attorneys/Agents For Applicant